**The Communication of March 21, 2006 and Reply**

*Claims 1-18 are rejected under U.S.C. 112, first paragraph, as based on a disclosure, which is not enabling. The MMA.exe computer program is critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See In re Mayhew, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). It is improper to incorporate by reference essential subject matter.*

Reply: Under the Examination Guidelines for Computer-Related Inventions issued by the US Patent and Trademark Office in 1996, the MMA.exe computer program is not included in the claims, and the flow diagrams of the program and the descriptions of the desired functions are included in the claims. It is noted that the flow diagrams and descriptions are well within the skill of a programmer in art to create said computer program to be installed into a general purpose digital computer device to accomplish the required calculations of the method of this invention. Therefore, the MMA.exe computer program is not included in the claims (Detailed description is presented in the Reply Form page 13, Reply 1 of the facsimile transmission).

*The attempt to incorporate subject matter into this application by reference to MMA.exe is ineffective because it does not enable one skilled in the art to practice the claimed invention.*

Reply: Under the Examination Guidelines, one skilled in the art practices the claimed invention by performing said MMA.exe computer program on said computer device, as disclosed in the claim 1-18 (Detailed description is presented in the Reply 1).

*The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the office.*

Reply: The references [1] to [22] on pages 3 to 5 of the specification have been amended by the none-patent documents 1-25 on pages 3 to 6 of the amended specification (Detailed description is presented in the none-patent documents on replacement pages 26 to 29 of the facsimile transmission).

*The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).*

Reply: The applicant has stated that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. The statement is presented in page 2 of the facsimile transmission.

*Claims 1-18 are rejecte under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and /or use the invention.*

Amendment: The claim(s) contains subject matter has been described in the amended specification (Detailed description is presented in the amendment

form pages 22 to 24, lines 63 to 99 of the facsimile transmission).

*In In re Wands (8 USPQ2d 1400 (CAFC 1988)), the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quality of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. In considering the factors for the instant claims:*

Reply: The eight factors to be considered in a determination of "undue experimentation" are unnecessary considerations for the claimed invention because one skilled in art does not practice any experimentation and the person practices the claimed invention by performing said MMA.exe computer programs on said computer device, as disclosed in the claims 1-18 and examples 1-5 of the specification (Detailed description is presented in the Reply Form pages 14 to 15, Reply 2 of the facsimile transmission).

*a) In order to use the claimed invention, one of skill in the art must be able to determine normal range of values for all of the atherosclerotic parameters. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.*

Reply: The disease risks yielded by all of the atherosclerotic parameters have been integrated into a total disease risk to be considered in a range with the seven sublevels by means of formulas (1)-(10) of the specification. Therefore, determining normal range of values for all of the atherosclerotic

parameters is an unnecessary consideration for the claimed invention. (Detailed description is presented in the Reply 2).

*b) The description describes papers, which have come out with guidelines that have defined acceptable levels for some of the parameters. For example, the LDL and CRP parameters have disclosed ranges of levels and have a corresponding disease risk level based on this range.*

Reply: Major clinical and experimental evidences have stated that early atherosclerotic lesions are caused by the mass transport of circulating LDL and monocytes from the blood phase into the lesion phase. Based on the evidences, the total disease risk to be considered in a range with the seven sublevels is produced by using the ranges of LDL and monocyte-related CRP levels in the blood, as disclosed on page 13, paragraphs [0014] to [0017] and pages 26 to 28, paragraph [0042] of the specification.

*The description does not provide detailed guidance as to the actual acceptable range of values used for all of the atherosclerotic parameters or the corresponding disease risk levels for all of the atherosclerotic parameters. For example, the radius of arterial vessels and axial positions are two additional parameters used to assess CHD risk.*

Reply: The disease risks yielded by all of the atherosclerotic parameters have been integrated into a total disease risk to be considered in a range with the seven sublevels by means of formulas (1)-(10) of the specification. Therefore, the actual acceptable range of values used for all of the atherosclerotic parameters including the radius and axial position parameters is an unnecessary consideration for the claimed invention (Detailed description is

presented in the Reply 2).

*However, "it can be concluded that the morphology of the vertbro-basilar junction as well as the morphology of the basilar artery is vary variable amongst adults." (Ravensbergen et al.).*

Reply: The angle parameter between gravity and mean velocity of blood fluid in arterial vessels is independent of the morphology, as indicated in a typical figure of the morphology (the PLATE 9A in Hemodynamic basis of atherosclerosis by Texon, Hemisphere Publishing Corporation, 1980). The morphology may influence the stress fields at the basilar area. A copy of the PLATE 9A figure has enclosed on the page 19 of the facsimile transmission.

*What is the acceptable range of normal values of arterial vessels and axial positions?*

Reply: The disease risks yielded by all of the atherosclerotic parameters including arterial radii and axial position parameters have been integrated into a total disease risk to be considered in a range with the seven sublevels. Therefore, the acceptable range of normal values of arterial radii and axial positions is an unnecessary consideration for the claimed invention (Detailed description is presented in the Reply 2).

*In addition, the inventor states that, "no screening method is able to determine the contribution of the arterial geometry to the disease." (Wang et al.).*

Amendment: the current screening method such as screening LDL or cholesterol level in the patient's blood is unable to determine the contribution of the arterial geometry to the disease (see the Amendment Form page 24, lines 108 to 112 of the facsimile transmission).

*With regards to those parameters disclosed, "observations suggest that the most recent National Cholesterol Education Program Adult Treatment Panel III guidelines, with LDL-C targets of 2.6 mmol/L, may result in under-treatment of a significant number of patients." (Evans et al.) Therefore, what is the acceptable range of LDL levels that would be considered normal and address this problem? Additionally, "many individuals who have CHD do not have substantially elevated LDL-C but have derangement of other lipid fractions." (Ballantyne et al.)*

Reply: The disease risks yielded by all of the atherosclerotic parameters including LDL level parameter have been integrated into a total disease risk to be considered in a range with the seven sublevels. Therefore, the acceptable range of LDL level parameter is an unnecessary consideration for the claimed invention (Detailed description is presented in the Reply 2 and the Reply form page 18, Reply 5 of the facsimile transmission).

*c) The description provides working examples of identification of connectron symmetries in genomic sequences. The description does not provide working examples of using identified connectron symmetries to predict effects on gene expression.*

Reply: The description does not provide working examples of using identified connectron symmetries to predict effects on gene expression because the angle parameter between the gravity and mean velocity of blood fluid in arterial vessels is independent of gene expression. The studies on relationships between the gene expression and shear stress acting at the inner arterial wall of lesion-prone sites, such as the shear stress-regulated gene, have reported by Libby (see reference [9] of the specification).

*d) The nature of the invention, CHD diagnosis, prediction, or treatment, is complex.*

Reply: The claimed invention is an efficient and reliable screening method and it can be well-used for diagnosis, prevention or treatment of atherosclerosis-related CHD, which is supported by major clinical and experimental evidences (Detailed description is presented in the Reply form pages 15 to 18, Replies 3 and 4 of the facsimile transmission).

*e) The prior does show a high level of unpredictability with regards to the parameters, a, Z, and alpha.*

Reply: The experimental and clinical studies have stated that the parameters, a, Z, and alpha associated with atherosclerosis (the references 1, 12, 13 and 14 of the specification). The macroscopically constant quantity of these parameters may be exactly measured by using medical technologies such as Computed Tomography and Intravascular Ultrasound (see the Reply 2).

*In addition, the prior shows a high level of unpredictability with regards to detecting CHD based on LDL levels.*

Reply: Traditional detection of CHD based on LDL levels is performed by determining the LDL level in an individual's blood. The method of screening LDL levels is unable to determine either the different amounts of disease risk yielded by different elevated LDL levels or the disease risk levels caused by other risk factors such as elevated CRP levels and hypertension, which results in a high level of unpredictability with regards to detecting CHD based on LDL levels (Detailed description is presented in the Reply 5).

*f) The skill of those in the art of CHD prediction and treatment is high.*

Reply: The specification has recited strong evidences that the claimed invention can be well-used for the diagnose, prediction or treatment of atherosclerosis-related CHD (Detailed description is presented in the Reply 4).

*g) The predictability of the relationship between some of the atherosclerotic parameters and CHD is unknown in the prior art.*

Reply: The traditional screening methods for atherosclerosis-related CHD are unable to determine the disease risks levels based on atherosclerotic parameters and their combined levels, which results in unknown predictability of the relationship between some of the atherosclerotic parameters and CHD in the prior art. The claimed invention can be used to determine and combine these levels, as indicated in examples 1-5 of the specification (Detailed description is presented in the Replies 4 and 5).

*h) The claims are broad in that they are drawn to diagnosing, preventing, or treating CHD.*

Reply: The claimed invention can be well-used to diagnose, prevent, or treat CHD, as disclosed in the example 1-5 of the specification (Detailed description is presented in the Reply 3 and 4).

*The skilled practitioner would first turn to the instant description for guidance in using the claimed invention. However, the description lacks clear evidence that all the atherosclerotic parameters can be used to diagnose, prevent, or treat CHD. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not disclose detailed guidance for a range of values for all the atherosclerotic parameters. Finally, said practitioner would turn to trial and error experimentation to determine a*

*relationship between the parameters and diagnosis, prevention, or treatment. Such, amounts to undue experimentation.*

Reply: The specification recites strong evidences that the claimed invention and all the atherosclerosis parameters can be well-used to diagnose, prevent or treat atherosclerosis-related CHD and this invention greatly improves current screening capabilities. These evidences are presented in the Reply Form pages 15 to 18, Replies 3 to 5 4 of the facsimile transmission.

*Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.*

*Claim 1 recites the limitation "normal" in line 9. There is insufficient antecedent basis for this limitation in the claim.*

Amendment: The "normal" has been described in the amended paragraph [0012] of the specification (Detailed description is presented on the Amendment Form page 23, lines 69 to 71 of the facsimile transmission).

*Claim 1 recites the limitation "the measured values" in line 25. There is insufficient antecedent basis for this limitation in the claim.*

Amendment: The "the measured values" has been described in the amended paragraph [0012] of the specification (Detailed description is presented on the Amendment Form page 23, lines 72 to 73 of the facsimile transmission).

*In claim 1, parameters v and u are vague and indefinite as to their precise meaning. Claim 1 recites the parameters of v and u as being "the variables related to said p and said a." However, the relationship between*

*these parameters remains unclear and is deemed vague and indefinite. Therefore, clearer claim wording is required.*

Amendment: The amended parameters v and u are presented on the Amendment Form page 21, lines 29 to 31 of the facsimile transmission.

*In claim 1, the parameter g has no specific unites and therefore is not clearly defined and remains vague and indefinite. Clearer claim wording is required.*

Amendment: The amended parameter g is presented on the Amendment Form page 21, lines 32 to 33 of the facsimile transmission.

*In claim 1, the parameter a, the radius parameter of arterial vessels, is vague and indefinite with regards to where this measurement or parameter value is obtained along the arterial pathway. In addition, the parameter alpha, the angle parameter of arterial vessels in degree and Z, the axial position of diffusional flux are also vague and indefinite with regards to where this measurement or parameter value is obtained along the arterial pathways. Therefore, clearer claim wording is required.*

Amendment: The amended parameters a, alpha and Z are presented on the Amendment Form page 20, lines 12 to 18 of the facsimile transmission.

*Claims 2-18 are rejected due to their dependence from a rejected claim and including issues from claim 1.*

Amendment: The amended Claim 1 is presented on the Amendment Form page 20 to 22, lines 3 to 49 of the facsimile transmission.

## Reply Form

The disease refers to atherosclerosis-related coronary heart disease or strokes (ACS) in this form.

**Reply 1.** Under the Examination Guidelines for Computer-Related Inventions issued by the USPTO in 1996, the MMA.exe computer program is not included in the claims, and the flow diagrams of the program and the descriptions of the desired functions are included in the claims. The flow diagrams are outlined on pages 37 to 39, lines 22 to 62 in claim 1. This diagrams are described in detail on pages 40 to 52, lines 71 to 336 in claims 2-16, including the following steps: calculating the disease risk amounts yielded by the nine atherosclerotic parameters or various risk factors by means of formulas (1)-(10) in claims 2-10; calculating a total disease risk in claim 11; determining a disease risk level in claim 12; determining a primary therapeutic target in claim 13; determining a primary cause in the disease in claim 14; determining a secondary therapeutic target in claim 15 and calculating a therapeutic efficacy in claim 16. It is noted that the flow diagrams and descriptions of desired functions in great detail are well within the skill of a programmer in art to create said computer program to accomplish the required calculations of the method of this invention. Therefore, the MMA.exe computer program is not included in the claims. This program is installed into a general purpose digital computer device so as to allow one skilled in the art to practice the claimed invention by performing said program on said computer device, as disclosed in claim 18 and the examples 1-5 of the specification (see the Examples: Mutual Fund and Matrix, etc. of said Examination Guidelines, claims 1-18 and the pages 30 to 34, paragraphs [0050] to [0064] in the specification).

**Reply 2.** The eight factors to be considered in a determination of "undue experimentation" are unnecessary considerations for the claimed invention because one skilled in art does not practice any experimentation and the person practices the claimed invention by performing said MMA.exe computer program on said computer device, as disclosed in claims 1-18 and the examples 1-5 of the specification.

The disease risks yielded by all of the atherosclerotic parameters have been integrated into a total disease risk to be considered in a range with the seven sublevels by means of formulas (1)-(10) of the specification. Therefore, the determination of range of normal or measured values for all the atherosclerotic parameters is an unnecessary consideration for the claimed invention. (see pages 18 to 28, paragraphs [0031] to [0042] of the specification).

The normal values of the nine atherosclerosis parameters are presented in claim 2-10. These values are based on current available standards from clinical literature and national studies. These values are subjected to change as standards to be updated and may vary from country to country (see pages 3 to 4, references 4 to 7 of the specification). These values may be determined by the physician. For example, the page 32, example 3 of the specification wherein the rate 1% reduction in the LDL level may be a rate between the LDL normal and measured values to be determined by the physician.

All of the atherosclerotic parameters have been measured by using medical technologies over the past decade. The radius, angle and diffusion length parameters may be exactly measured by using medical technologies such as Computed Tomography (CT) and Intravascular Ultrasound (IVUS), various medical technologies are available for a determination of CRP parameter such as Immunoturbidimetry, Rapid Immunodiffusion and Visual Agglutination, and

other five atherosclerotic parameters of LDL levels, blood systolic and diastolic pressure, plasma/blood temperature and heart rate as the routine testing items are available in most hospitals or medical centers in the United States.

The molecular biology is closely related to experimental studies in producing reliable results. The studies concentrate on the understanding of macromolecules and the macromolecular mechanisms found in living things. For example, the molecular nature of the gene and its mechanisms of gene replication, mutation, and expression. The eight factors summarized by the CAFC are used for the determination of "undue experimentation" in the experimental studies of molecular biology. The eight factors are unnecessary considerations for the instant claims because the experimenal technology for the understanding of macromolecular mechanisms such as exploring the molecular nature of genes is unsuitable for the measurement of the nine atherosclerotic parameters such as blood pressure and radius parameters.

The measured and normal values of said nine atherosclerotic parameters are a set of inputting data of said MMA.exe computer program. Under said Examination Guidelines, the inputting data are received or provided and the issue of experimentation regarding these data is not described in the flow diagrams of the claims (see the Examples of said Examination Guidelines).

**Reply 3**. The claimed invention is a reliable screening method for ACS. Major clinical and experimental evidences (Lusis, Atherosclerosis, Nature, 2000, Vol.407, 233-241) have stated that early atherosclerotic lesions consist of the subendothelial accumulations of foam cells formed by the circulating LDL particles and monocyte cells. These particles and cells are transported from the blood phase into the lesion phase. The mass transport of blood constituents obeys

the conservation principles of mass, momentum and energy because the blood fluid in circulating system obeys these principles (see the page 3, reference [1] of the specification). These evidences indicate that the lesions are formed by LDL and monocyte accumulations in the subendothelium, not the LDL and monocytes in blood. Based on these evidences, the claimed invention treats the mass transfer flux of equations (1.1) in the specification as a primary cause in the disease because it is a resource for the LDL and monocyte accumulations in the subendothelium (see the reference [1]). The claimed invention is a reliable screening method for ACS because it is strongly supported by the major clinical and experimental evidences and the three conservation principles (see the pages 3 to 5, references [1], [9], [18] to [19] and pages 13 to 14, paragraphs [0014] to [0019] of the specification)

The claimed invention is an efficient screening method for ACS. The epidemiology studies have identified many risk factors associated with ACS, including the elevated LDL or CRP levels in blood, hypertension and smoking cigarette, etc. These studies indicate that ACS is a multifactor disease with differently combined risk factors dominating in different individuals. The current screening methods for ACS are unable to determine different disease risk levels yielded by different risk factors and combine the levels because these methods treat single risk factor such as the elevated LDL or CRP levels as a primary cause in the disease. Based on the studies, the method of this invention treats the mass transfer flux, a combined risk factor, as a primary cause in the disease, and the disease risks yielded by various risk factors have been integrated into the flux by means of the nine atherosclerotic parameters and equations (1.2) and (1.3), so that the claimed invention can be used to predict a total disease risk, assess a therapeutic efficacy and determine therapeutic targets, as disclosed in example 1-

5 of the specification. These results indicate that the claimed invention is an efficient screening method for ACS because and greatly improves the current screening capabilities (see the pages 3 to 5, references [4], [9] and [19]; page 8, paragraph [0006]; pages 16 to 29, paragraphs [0025] to [0047]; and pages 30 to 34, examples 1-5 of the specification).

**Reply 4.** The specification recites the strong evidences that the claimed invention can be well used to diagnose, prevent or treat ACS and greatly improves the current screening capabilities. These evidences are briefly summarized as follows:

The clinical and experimental evidences (the references [3] to [8], [18], [20], [24] and [25] of the specification) indicate that the method of screening LDL or cholesterol levels in patients' blood is widely used to diagnose, prevent or treat ACS over the past several decades. The clinical and physiology studies (the references [9], [10] and [19]) state that the method of screening plasma CRP levels can be well used for the diagnosis, prevention and treatment of ACS. These evidences strongly support that the claimed invention can be well used to diagnose, prevent or treat ACS because the two methods of screening LDL and CRP levels have been united into this invention by means of equation (1.1) and formulas (1)-(3) of the specification.

The epidemiological, clinical and experimental studies (the references [3] to [10], [18] and [19] of the specification) have identified many risk factors associated with ACS, mainly including elevated LDL levels, hypertension, system inflammation related elevated CRP levels, smoking cigarette and family history, etc. These risk factors have been widely used for the diagnosis, prevention or treatment of ACS but they cannot be united. These evidences strongly support that the claimed invention can be well used for the diagnosis,

prevention or treatment of ACS because these risk factors have been united into the invention through the nine atherosclerotic parameters. These parameters can be well used to the diagnosis, prevention or treatment of ACS because they are closely relate to these risk factors, as disclosed in the paragraphs [0027] and [0028] of the specification. The method of this invention can be used to predict a total disease risk, assess the therapeutic efficacy and determine therapeutic targets for the individual who require the diagnosis, prevention or treatment of ACS, as indicated in the examples 1-5 of the specification, which greatly improve the current screening capabilities (Detailed descriptions are presented in pages 3 to 5, references [3] to[10], [18] to [20], [24] and [25]; pages 6 to 9, paragraphs [0003] to [0006]; and pages 15 to 35, paragraphs [0021] to [0070] of the specification).

Reply 5. Current screening methods for ACS treat a single risk factor as the primary cause in the disease. The methods are unable to determine different disease risk levels yielded by different risk factors and combine the levels. For example, the LDL screening method is used to determine the LDL or cholesterol level in patients' blood, not the disease risk levels; thus it is unable to determine the different disease risk levels yielded by different amounts of elevated LDL levels or the disease risk levels caused by other risk factors such as elevated CRP levels, which results in limited clinical screening capabilities. Lusis emphasizes that efficient screening procedures are urgently needed (Nature, 2000, Vol.407, page 241). The claimed invention treats the mass transfer flux as a primary cause in the disease and it can be used for quantitative calculations of disease risk amounts yielded by various risk factors and the combination of the amounts, as disclosed in the pages 30-34, example 1-5 of the specifications.

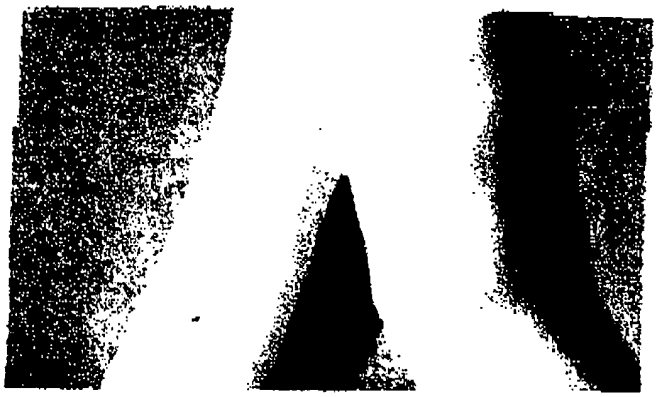

PLATE 9A

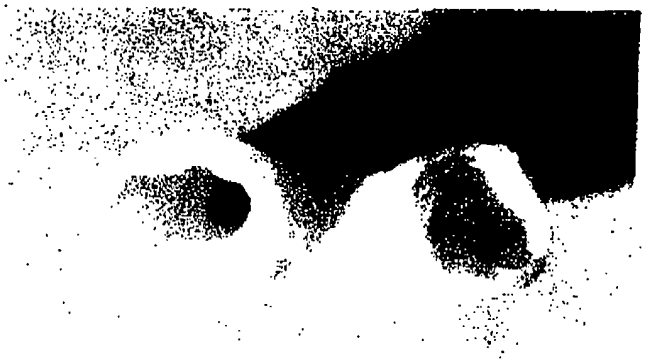

PLATE 9B

PLATE 10A

**Amendment Form**

The following symbol " " refers to the paragraphy or words being amended or inserted.

1. Claim 1 is to be amended as follows:

(a) Original location: page 37, lines 16 to 21 of Claim 1.

Original: "a = the radius parameter of arterial vessels in cm, T = the temperature parameter of blood plasma in °C, α = the angle parameter of arterial vessels in degree and z = the axial position parameter of diffusional flux in cm, called diffusional length;"

Amendment: "a = the radius parameter in arterial radius in cm, T = the temperature parameter of blood plasma in °C, α = the angle parameter between the gravity and mean velocity of blood fluid in arterial vessels in degree and z = the length parameter of diffusion flux along the inner wall in the axial direction of arterial vessels in cm;

(b) Original location: page 38, lines 30 to 35 of Claim 1.

Original: "wherein J = the mass transfer flux in

$10^{-5}$ g/($cm^2$s), A, B and E = the variables that are independent of said atherosclerotic parameters, v and u = the variables related to said p and said a, D = the diffusion coefficient in $cm^2$/s, and g = the gravitational acceleration;"

Amendment: "wherein J = the mass transfer flux in $10^{-5}$ g/($cm^2$s), A, B and E = the constants of conversion factors, v = the eddy velocity of blood fluid in arterial vessels in cm/s, u = the mean velocity of the blood fluid in cm/s, D = the diffusion coefficient in $cm^2$/s and g = the gravitational acceleration in $cm/s^2$;"

(c) Original location: page 38, lines 36 to 37 of Claim 1.

Original: "determining the normal values of said atherosclerotic parameters;"

Amendment: "providing the normal values of said atherosclerotic parameters;"

(d) Original location: page 40, lines 68 to 70 of the claim 1.

Original: "above-mentioned said methods are written as an executable computer program named the MMA.exe © 2004, by Xing F. Wang to perform said

methods."

Amendment: "above-mentioned said methods are written as an executable computer program named the MMA.exe to be installed into a general purpose digital computer device to accomplish said methods."

2. Claim 18 is to be amended as follows:
Original location: page 52, lines 343 to 346 of claim 18.

Original: "A method as in claim 1 wherein said method in claim 2 through said method in claim 16 are written as an executable computer program named said MMA.exe to perform said methods which comprises:"

Amendment: "A method as in claim 1 wherein said method in claim 2 through said method in claim 16 are written as an executable computer program named the MMA.exe to be installed into a general purpose digital computer device to accomplish said methods comprising;"

3. The paragraphy [0012] of the specification is to be amended as follows:
(a) Original location: page 11, lines 13 to 14 of the specification.

Original: "an individual having the measured values of atherosclerotic parameters;"

Amendment: "defining the normal as free from atherosclerosis-related coronary heart disease or stroke;

the measured values refer to the quantities of atherosclerotic parameters to be measured;

an individual having the measured values of atherosclerotic parameters;

providing the normal values of said atherosclerotic parameter;"

(b) Original location: page 12, lines 21 to 23 of the specification.

Original: "the above-mentioned methods are written as an executable computer program named the MMA.exe to perform said methods."

Amendment: "the above-mentioned methods are written as an executable computer program named the MMA.exe to be installed into a general purpose digital computer device to accomplish said methods."

4. The paragraph [0048] of the specification is to be amended as follows:

Original location: page 29, lines 18 to 21 of the

specification.

Original: "These methods in Step three through Step nine are written as an executable computer program named said MMA.exe that provides greater ease and convenience to perform these methods."

Amendment: "These methods in Step three through Step nine are written as an executable computer program named the MMA.exe to be installed into a general purpose digital computer device to accomplish these methods."

5. The paragraph [0059] of the example 4 of the specification is to be amended as follows:

Original location: page 33, lines 1 to 2 of the specification.

Original: "no screening method is able to determine the contribution of the arterial geometry to the disease."

Amendment: "the current screening methods such as screening LDL or cholesterol levels in the patient's blood are unable to determine the contribution of the arterial geometry to the disease."

6. The references [1] to [22] on pages 3 to 5 of the

specification have been amended by the none-patent documents 1 to 25 on pages 3 to 6 of the amended specification consist of the pages 26 to 29 of the facsimile transmission.

The 13 replacement sheets including the pages 37, 38, 40 and 52 of the amended claims and the pages 3 to 6, 11, 12, 13, 29 and 33 of the amended specification consist of the pages 26 to 37 of the facsimile transmission.